REMARKS

Claims 1-49 are pending. Claims 9-43 are withdrawn from further consideration as being drawn to non-elected inventions. Claims 1-8 and 44-49 are under examination. Claims 1-8 and 44-49 have been amended to clarify the invention. New claims 50-57 have been added. The new claims merely further clarify the scope of the invention.

Applicants respectfully assert that all amendments and new claims are supported by the original disclosure and do not introduce new matter. Moreover, Applicants further respectfully assert that the amendments merely clarify the scope of the claims.

Restriction

Earlier, Applicants elected, with traverse, Group I (claims 1-8 and 44-49) and SEQ ID NO.2. Examiner has now indicated that SEQ ID NOS.1 and 2 are to be examined together. Applicants appreciate Examiners consideration on this matter.

The Examiner has objected to the disclosure because it contains an embedded hyperlink and/or other form of browser-executable code)see page 13, line 18, for example). Examiner has instructed that Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code found through the specification per MPEP § 608.01. Applicants have amended the specification to remove any hyperlinks.

The Examiner has objected to claim 5 because it depends on itself. Applicants have now amended claim 5 to provide for proper dependency.

Claim Rejections - 35 USC §112, 1st paragraph

Examiner has rejected claims 1-8 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner contends that the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reciting the term "an inner

leaflet component", and "a prosaposin-related polypeptide comprising an amino acid sequence having 80% identical to SEQ ID NO.1 or 2.

The specification teaches that the "inner leaflet component" refers to any molecule or structural analog thereof naturally occurring in the inner leaflet of a plasma membrane of a cell, particularly an animal cell, more particularly a mammalian cell (see page 4, paragraph [0012], lines 3-6). The written description in this instant case only sets forth anionic phospholipid, particularly phosphatidylserine, SEQ ID NO.1 and SEQ ID NO.2. Therefore the written description is not commensurate in scope with the claims which read on any and all inner leaflet component, and any and all sequences that are at least 80% identical to SEQ ID NO.1 or 2.

Applicants have now amended the claims to meet the written description requirement for a claimed genus through limiting the claimed invention to structures having identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, and by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus.

The claims are now limited to a composition comprising an inner leaflet component, wherein the inner leaflet component is a phospholipid selected from the group consisting of phosphatidylserine, phosphatidylethanolamine, and structural analogs thereof, a prosaposin-related polypeptide, wherein the polypeptide has an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence set forth in SEQ ID NO:1;

(b) an amino acid sequence substantially identical to the amino acid sequence set forth in SEQ ID NO:1 having 80% sequence identity to the amino acid sequence set forth in SEQ ID NO:1, wherein said polypeptide retains plasma-membrane affinity;

(c) the amino acid sequence set forth in SEQ ID NO:2; and

(d) an amino acid sequence substantially identical to the amino acid sequence set forth in SEQ ID NO:2 having 80% sequence identity to the amino acid sequence set forth in SEQ ID NO:2, wherein said polypeptide retains plasma-membrane affinity; and

a pharmaceutically acceptable carrier;

wherein the percentage of sequence identity is determined by a sequence comparison program equivalent to the GCG program GAP (Version 10.00 or later) wherein the comparison window is at least 20 contiguous amino acids in length; and

wherein the prosaposin related polypeptide and the inner leaflet component form a nanovesicle.

Applicants respectfully traverse this rejection in light of the showing of working examples in the specification, the predictability of the art for the claim scope, the correlation of working examples of the claimed invention, the correlation of working examples in the prior art to the claimed invention, and the correlation of animal models to the disease.

Applicants have provided sufficient detailed examples in the specification showing peptides comprising less than the full amino acid protein depicted in SEQ ID NO:1 and 2. The U.S. Patent Office clearly does not require a description of every embodiment for peptide claims and that while protein chemistry taken as a whole may be unpredictable, particular embodiments are patentable. Applicants have provided sufficient detail of particular patentable embodiments.

Because of the unpredictability of living processes, generic biological claims inherently must cover inoperative members of the class. This is not fatal to the claim if a person skilled in the art can recognize which species are operative and which are not, especially if functional limitations are used to exclude inoperative members. In the present case, inoperative members are specifically excluded through the functional limitations that the polypeptide must retain plasma-membrane affinity.

Any person skilled in the present art can easily ascertain the sequences that fall within the scope of the present claims. The scope of the claims requires that the sequence is 80%wherein the percentage of sequence identity is determined by a sequence comparison program equivalent to the GCG program GAP (Version 10.00 or later) wherein the comparison window is at least 20

contiguous amino acids in length. Therefore, sequence that does not meet these criteria will inherently fall outside the scope of the present claims.

The Examiner has also rejected claims 1-8 under 35 U.S.C. 112, first paragraph, contending that the specification, while being enabling for an agent comprising an anionic phospholipid, particularly phosphatidylserine and a prosaposin polypeptide of SEQ ID NO.1 or SEQ ID NO.2, does not reasonably provide enablement for an agent comprising any and all inner leaflet component, and any and all prosaposin-related polypeptide of an amino acid sequence that is at least 80% identical to SEQ ID NO.1 or 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As stated above, Applicants contend that the claims, as now amended, are fully enabled. Applicants respectfully submit that the specification provides adequate direction to those skilled in the art and that the disclosure would not require undue experimentation.

Thus, is respectfully submitted that the present specification fully meets the requirements of 35 U.S.C. 112 and withdrawal of these rejections is respectfully requested.

Claim Rejections - 35 USC § 102

The Examiner has rejected claims 1-8 and 44-49 under 35 U.S.C. 102(b) as being anticipated by Morimoto et al. (J. Bio. Chem., 1990, 265(4): 1933-1937), and as evidenced by Morimoto et al. (Proc. Natl. Acad. Sci. U.S.A., 1989: 86: 3389-3393).

The Examiner contends that Morimoto et al. teach an agent (an assay mixture) comprising saposin C, dioleoylphosphatidylserine and glucosylceramidase (see page 1933, under materials, and page 1934, 1st paragraph). The concentration of saposin C is from 0-20 μM (see Fig.2), and of phosphatidylserine is from 0-200 ^M (see Fig. 3). The mass ratio of saposin C (7 (ag or 10 (ig) to dioleoylphosphatidylserine (0.65 nmol is 0.5 ng) is about 13:1 or 20:1, and the molar ratio of saposin C to dioleoylphosphatidylserine is about 1:1-1:10 (see page 1934, left column, under Results, lines 15-16, Fig. 1, column 7). The mass ratio of saposin C to dioleoylphosphatidylserine can also be about 1:1 (see Fig.2 and Fig.3). The sequences of the

saposin C and A of Morimoto et al. are 100% identical to the instant SEQ ID NO.1 or 2 (see page 1933, right column, under materials, lines 1-2), as evidence by Morimoto et al. (PNAS USA, 1989, 36:3389-3393) and the sequence alignment (see Exhibit A). Morimoto et al. teach the pharmaceutical carrier e.g. acetate buffer (see page 1934, left column, line 6).

The Examiner contends that although Morimoto et al. do not teach that the agent comprising saposin C and dioleoylphosphatidylserine have anti-tumor activity or promotes death in cancer cells, the claims are drawn to a product per se and inherently, such an agent would have anti-tumor activity.

Applicants contend that the rejections under 35 U.S.C. 102 is not applicable to the claims of the present invention, as amended herein.

Applicants assert that the present invention, as embodied in the currently amended claims, are patently distinct from the teachings of Morimoto. The present invention provides for an inner leaflet component, biologically active portion of a prosaposin-related polypeptide and a pharmaceutically acceptable carrier wherein the prosaposin related polypeptide and the inner leaflet component form a nanovesicle. In such nanovesicles, the polypeptide is embedded within the lipid membrane by dynamic processes of saposin interactions with phospholipid membrane.

The teaching of Morimoto shows the sequential addition of ingredients and does not teach the preparation of the nanovesicles having the polypeptide complexed with the membrane of the nanovesicles necessary for the present invention.

Claim Rejections - 35 USC § 103

The Examiner has rejected claims 1-8 and 44-49 under 35 U.S.C. 103(a) as being unpatentable over Vaccaro et al. (FEBS 1993, 336(1): 159-162) in view of the teachings of O'brien et al. (WO9503821A1).

Vaccaro et al. teach an agent (an assay mixture) comprising saposin C, dioleoylphosphatidylserine and glucosylceramidase (see page 160 paragraph 2.5, and page 159, under materials, line 5). The concentration of saposin C is from 0-25 jug/ml (see Fig.1). The

amount of phosphatidylserine is from 0-80 μg (see Fig. 1, 2 and Table 1). The mass ratio of saposin C to dioleoylphosphatidylserine is about 1:3 or 5:1 (see Table 1 ; and Fig.2). The molar ratio of saposin C to dioleoylphosphatidylserine is about 1:1-1:10 (after calculation). Vaccaro et al. teach the pharmaceutical carrier e.g. acetate buffer (see page 160, paragraph 2.5).

Applicants assert that the present invention, as embodied in the currently amended claims, are patently distinct from the teachings of Vaccaro et al. in view of the teachings of O'brien et al. The present invention provides for an inner leaflet component, biologically active portion of a prosaposin-related polypeptide and a pharmaceutically acceptable carrier wherein the prosaposin related polypeptide and the inner leaflet component form a nanovesicle. In such nanovesicles, the polypeptide is embedded within the lipid membrane by dynamic processes of saposin interactions with phospholipid membrane.

Applicants contend that the rejections under 35 U.S.C. 103 is not applicable to the claims of the present invention, as amended herein.

Double Patenting

Claims 1-3 and 44-47 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 16, 17, 21 and 22 of U.S. Patent No. 6,872,406 in view of Vaccaro et al. (FEES Lett. 1994, 349: 181-186, IDS).

Claims 1-3 and 44-47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16, 17, 21 and 22 of copending Application No. 10/967,921 in view of Vaccaro et al. (FEBS Lett. 1994, 349: 181-186, IDS). Although the conflicting claims are not identical, they are not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants assert that they will file a Terminal Disclaimer (and filing fee) assuring that the present application and copending Application No. 10/967,921 will expire at the same time if conflicting claims are issued. The filing of this Terminal Disclaimer should render moot the double patenting rejection.

Accordingly, it is submitted that the rejections under 35 U.S.C. 103 is not applicable to the claims of the present invention, as amended herein, and it is respectfully requested that they be withdrawn.

In light of the amendments and remarks made herein, it is respectfully submitted that the claims currently pending in the present application are in form for allowance. Accordingly, reconsideration of those claims, as amended herein, is earnestly solicited. Applicants encourage the Examiner to contact their representative, Stephen R. Albainy-Jenei at (513) 651-6839 or salbainyjenei@fbtlaw.com. The Commissioner for Patents is hereby authorized to charge any deficiency or credit any overpayment of fees to Frost Brown Todd LLC Deposit Account No. 06-2226.

Respectfully submitted,

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